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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,993	09/07/2006	Satoshi Kanazawa	80186(302730)	6413

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,993	KANAZAWA ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5 and 11-17* is/are pending in the application.

4a) Of the above claim(s) *11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 30 April 2009.

Claim Status

Claims 1, 2, 5 and 11-17 are pending. Claims 3-4 and 6-10 are cancelled. Claims 11-17 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1, 2, and 5 are amended. Claims 1, 2 and 5 are under current examination.

Priority

This application claims benefit from PCT/JP2005/04007 (filed 8 March 2005). This application also claims benefit from foreign application, JAPAN 2004-066218 (filed 9 March, 2004). The instant application has been granted the benefit date, 9 March 2004, from the foreign application, JAPAN 2004-066218.

RESPONSE TO ARGUMENTS

Specification

The objection to the specification is withdrawn in response to the amended specification filed on 4/30/2009. The specification amendment has removed the embedded hyperlink found on page 7, line 32.

Claim Objections

The objection to claim 1, based on "parentheses," is withdrawn in response to the applicant's claim amendments.

35 USC § 112, 2nd paragraph

Claim Rejections - 35 USC § 112

The rejection of claims 3-8 under 35 USC 112, 2nd paragraph is withdrawn in response to the applicants claim amendments.

The applicant's claim amendments have been fully considered and are persuasive. The applicant has amended the claims so to remove the language deemed indefinite. There is perfect clarity regarding this word usage.

Therefore, the examiner hereby withdraws the rejection of claims 3-8 under 35 USC 112, 2nd paragraph.

35 USC § 112, 1st paragraph (scope of enablement)

The rejection of claims 1-10 under 35 USC 112, 1st paragraph (scope of enablement) is withdrawn in response to the applicants claim amendments and arguments.

The applicant's claim amendments have been fully considered and are persuasive. Claims 3-4 and 6-10 are cancelled. Therefore, the rejection of these claims is moot. The applicant has amended the claims 1, 2 and 5 so as to narrow the scope of the claims to a transgenic mouse or rat. The applicant has argued that the sequence and function of the CIITA gene and type II collagen promoter are well known in the art and are highly conserved between different species. Therefore, the applicant argues that a transgenic rat would be predictable based on the example of a transgenic mouse provided by the specification. The examiner finds this argument persuasive.

Therefore, the examiner hereby withdraws the rejection of claims 1-10 under 35 USC 112, 1st paragraph (scope of enablement).

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Fabre and Osaki

The rejection of claims 1-2 under 35 U.S.C. 103(a) as being obvious over Fabre et al. (WO98/15626) in view of Osaki et al. (Biochemical Journal. 11 September 2002; 1-34) is withdrawn in response to the applicants claim amendments and arguments.

The applicant's claim amendments have been fully considered and are persuasive. The applicant has amended the claims 1-2 by introducing a phenotype into claim 1. Since the cited art do not teach the claimed phenotype, the examiner finds this claim amendment sufficient to overcome the pending rejection.

Therefore, the examiner hereby withdraws the rejection of claims 1-2 under 35 U.S.C. 103(a) as being obvious over Fabre et al. in view of Osaki et al.

Harton, Lindqvist and Otten

Claims 1, 2 and 5 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Harton et al. (Molecular and Cellular Biology, Sept. 2000; 20(17):6185-6194) in view of Lindqvist et al. (Trends in Genetics. 2002; S7-S13) and further in view of Otten et al. (Journal of Immunology. 2003; 170: 1150-1157) for the reasons of record and the comments below.

The applicant's arguments and claim amendments have been fully considered but are unpersuasive. The applicant has cancelled claims 3-4 and 6-10; therefore the rejection of these claims is moot.

The applicant indicates that the three cited references are not anticipatory of the claimed transgenic mouse. The applicant, therefore, reasons that, "the combination of references fails to suggest the unexpected results achieved by the invention as now claimed" (Remarks, filed 4/30/2009, page 11, parag.2). Based on the applicant's discussion under the Fabre and Osaki obviousness rejection, the examiner is interpreting the "unexpected result" to be that symptoms of rheumatoid arthritis are induced by administration of at least two doses of 0.01mg to 0.05 mg of collagen to the transgenic mouse comprising a MCH class II transactivator gene operatively linked to a type II collagen promoter.

The examiner finds the applicant's argument unpersuasive. Harton teaches that increased expression of MHC class II transactivator induces pathological symptoms of Rheumatoid Arthritis. Otten teach a transgenic mouse expressing CIITA in all organs and further suggest this mouse is a model for RA. Lindqvist teach a transgenic mouse having cartilage-restricted expression based on a type II collage promoter. In addition, the cited art teaches criteria for classification and characterization of rheumatoid arthritis in mouse models of RA, such as those listed in claim 5. The important requirement for induction of RA symptoms in a transgenic mouse comprising CIITA gene seems to be expression of CIITA. Without evidence to the contrary, a skilled artisan would anticipate the type II collage promoter to be sufficient to produce enough CIITA to generate RA symptoms.

The applicant has introduced a reference (Kanazawa et al. PNAS, Sept 26, 2006; 103(39): 14465-14470) to substantiate the experimental results of the instant

application. The instant inventors are co-authors of the Kanazawa 2006 PNAS reference. In the Kanazawa reference and instant specification, the applicant has contrasted other mouse models of Rheumatoid Arthritis with the claimed mouse, in order to support the inventor's assertion that the claimed mouse has higher sensitivity to collagen. Based on the evidence provided, the examiner accepts that it is possible to induce symptoms of arthritis with the relatively low doses of collage now present in the claim. However, the examiner is left to ask himself, how has this knowledge advanced science or what is the inventive feature of inducing Rheumatoid Arthritis symptoms in a mouse, using only a low dose of collagen. After all, the use of the collage type II promoter was suggested in other mouse models of RA and transgenic mice overexpressing CIITA were generated by other groups and suggested as a model of RA. Taken as a whole, the examiner is not persuaded by the applicant's arguments regarding the secondary considerations; inducing RA symptoms in a transgenic mouse suggested by previous researches, using only a low dose of collagen, is insufficient to make the instant invention non-obvious.

Therefore, the examiner hereby maintains the rejection of claims 1, 2 and 5 under 35 U.S.C. 103(a) as being obvious over Harton et al. in view of Lindqvist et al. and further in view of Otten.

The examiner reiterates the pending rejection:

Claims 1, 2 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harton et al. (Molecular and Cellular Biology, Sept. 2000; 20(17):6185-6194) in

view of Lindqvist et al. (Trends in Genetics. 2002; S7-S13) and further in view of Otten et al. (Journal of Immunology. 2003; 170: 1150-1157).

Claim 1 is directed to a transgenic mouse or rat comprising a foreign DNA, the foreign DNA having a DNA which is selected form the group consisting of MHC class II transactivator gene, an active region of the MHC class II transactivator gene, and a mutant MCH class II transactivator gene (having a master switch function for controlling an expression of the MHC class II genes), and which is under the control of a type II collagen promoter.

Harton et al. teach class II MHC is involved in rheumatoid arthritis (page 6185, col.1, Introduction, lines 9-11) and CIITA expression is required for expression of class II MHC (page 6185, col.2, Introduction, lines 10-12). Harton et al. demonstrate the nexus between class II transactivator (CIITA) expression for the expression of class II MHC and its role with MHC in rheumatoid arthritis. Further, Harton suggests that enhancement of class II MHC through CIITA is involved in critical events of pathogenesis and autoimmune diseases such as RA (page 6191, col.1, last parag.).

Harton et al. does not teach a transgenic non-human mammal comprising CIITA operably linked to collage II promoter.

Lindqvist et al. teach a variety of mouse models of rheumatoid arthritis. In particular, Lindqvist et al. teach collagen induced arthritis (CIA), in which mice display symptoms similar to human rheumatoid arthritis when injected with type II collagen. Lindqvist et al. also teach in transgenic models of RA, the effect of a specific gene is evaluated for its involvement in the arthritis development (page S8, col.2). Lindqvist et

al. teaches "RA is genetically associated with the major histocompatibility complex (MHC) class II" (page S8, col.1, parag.1). Lindqvist et al. teach a transgenic mouse having cartilage-restricted expression based on a type II collage promoter (page S9, col.2 and Fig.1).

Lindqvist et al. does not teach a transgenic non-human mammal comprising CIITA operably linked to collage II promoter, but does suggest other transgenic animal models for RA, including some which have collagen-specific expression. Lindqvist et al. further teaches induction of RA symptoms in the CIA model. Lindqvist et al. also suggests making generic mouse models of RA by expression of "a specific gene." Finally, Lindqvist et al. teach the connection between MHC II expression and rheumatoid arthritis. Additionally, Lindqvist et al. teaches symptoms in mouse models of RA which correspond to claim 5 (Table 1); the list in claim 5 is commonly used to identify pathological conditions found in mouse models of RA and is therefore obvious.

Otten et al. teach "Increased CIITA and MHC-II expression...occur in autoimmune conditions such as rheumatoid arthritis" (page 1150, col.2, last parag.). Otten et al. also teach a transgenic mouse expressing CIITA in all organs (page 1153, col.1, parag.1). Otten et al. teach "[i]n our transgenic mouse, the CIITA transgene induces MHC-II expression in most cell types" (page 1156, col.2, CIITA transgenic mice section).

While Otten et al. emphasize the affect of CIITA overexpression on immune cell function, it is clear that their transgenic CIITA mouse is suggested as being a model of

rheumatoid arthritis. However, Otten et al. do not teach a transgenic non-human mammal comprising CIITA operably linked to collage II promoter.

However, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a transgenic non-human mammal comprising a foreign DNA, the foreign DNA having a DNA which is a MHC class II transactivator (CIITA) gene, and which is under the control of a type II collagen promoter.

The person of ordinary skill in the art would have been motivated to make a transgenic mouse comprising a MHC class II transactivator (CIITA) gene which is under the control of a type II collagen promoter. Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (transgenic mice comprising CIITA; nexus between CIITA expression and RA; animal models of RA which include administration of collagen II; and suggestions for joint-specific (collagen) expression of genes in animal models of RA) are taught by Harton or Lindqvist or Otten and further they are taught in various combinations and are shown to be used in mouse models of rheumatoid arthritis. It would be therefore predictably obvious to use a combination of these elements in a mouse models of rheumatoid arthritis.

The skilled artisan would have had a reasonable expectation of success in combining the teachings of Harton et al. and Lindqvist et al. and Otten because making

transgenic mice having tissue-specific expression patterns was known in the art at the time of the instant invention.

Therefore the transgenic non-human mouse as taught by Harton et al. in view of Lindqvist et al. and further in view of Otten et al. would have been *prima facie* obvious over the transgenic mouse having a phenotype of rheumatoid arthritis-like symptoms of the instant application.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
Patent Examiner, Art Unit 1633

/Joseph T. Woitach/
Supervisory Patent Examiner, Art Unit 1633